Cell Cycle 2011 vol.10 N23, pages 4090-4097

Sensitivity of acute myeloid leukemia Kasumi-1 cells to binase toxic action depends on the expression of KIT and AML1-ETO oncogenes

Mitkevich V., Petrushanko I., Spirin P., Fedorova T., Kretova O., Tchurikov N., Prassolov V., Ilinskaya O., Makarov A.
Kazan Federal University, 420008, Kremlevskaya 18, Kazan, Russia

Abstract

Some RNases selectively attack malignant cells, triggering an apoptotic response and therefore are considered as alternative chemotherapeutic drugs. Here, we studied the effects of Bacillus intermedius RNase (binase) on murine myeloid progenitor cells FDC-P1, transduced FDC-P1 cells ectopically expressing mutated human KIT N822K oncogene and/or human AML1-ETO oncogene and human leukemia Kasumi-1 cells expressing both of these oncogenes. Expression of both KIT and AML1-ETO oncogenes makes FDC-P1 cells sensitive to the toxic effects of binase. Kasumi-1 cells were the most responsive to the toxic actions of binase among the cell lines used in this work with an IC 50 value of 0.56 μM. Either blocking the functional activity of the KIT protein with imatinib or knocking-down oncogene expression using lentiviral vectors producing shRNA against AML1-ETO or KIT eliminated the sensitivity of Kasumi-1 cells to binase toxic action and promoted their survival, even in the absence of KIT-dependent proliferation and antiapoptotic pathways. Here, we provide evidence that the cooperative effect of the expression of mutated KIT and AML1-ETO oncogenes is crucial for selective toxic action of binase on malignant cells. These findings can facilitate clinical applications of binase, providing a useful screen based on the presence of the corresponding target oncogenes in malignant cells.

http://dx.doi.org/10.4161/cc.10.23.18210

Keywords

Apoptosis, Cytotoxic RNase, Imatinib, Myeloid progenitor cells, Oncogenes, ShRNA